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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,516	05/08/2001	John W. Lough JR.	650053.91134	4340

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EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/851,516	<b>Applicant(s)</b> LOUGH ET AL.	
	<b>Examiner</b> David S Romeo	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 5-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-21 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>05/08/2001</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Claims 1-21 are pending.

Applicant's election with traverse of group X, claims 1-4, to the extent that they  
5 are drawn to a composition comprising BMP-6 and FGF-4 in Paper No./the paper filed  
02/17/2004 is acknowledged. The traversal is on the following ground(s):

that restriction is optional;

that if the search can be made without serious burden the examiner must examine  
independent and distinct inventions;

10 that groups I-VII can be examined without serious burden;

that groups VIII-XIV can be examined without serious burden;

that groups XV-XXI can be examined without serious burden;

that groups XII-XXVIII can be examined without serious burden;

that groups XXIX-XXXIV can be examined without serious burden;

15 that groups XXXV-CXXXIX can be examined together and further with any of  
the other groups without serious burden;

that only a limited number of documents would be uncovered;

that the results of a search of the method claims is even more limited than the  
results of a search of the composition claims; and,

20 that more sophisticated searches conducted by the Office would uncover an even  
more limited number of documents.

This is not found persuasive because the inventions are independent and distinct,  
as set forth in the last Office action, and there is no claimed generic concept linking the

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independent and distinct inventions. As a result, the searches required for all of the independent and distinct inventions are non-overlapping, separate, and undue. Contrary to the number of results uncovered by Applicants, a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. Furthermore, a search of the claimed compositions is not limited to the “cardiogenic” art, and therefore requires a search of relevant literature in many different areas of subject matter.

The requirement is still deemed proper and is therefore made FINAL.

10

Claims 1-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), to the extent that they are drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 5-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No./the paper filed 02/17/2004.

15

Claims 1-4 are being examined to the extent they read upon a composition comprising BMP-6 and FGF-4.

20

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5

Claims 1, 3, 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wozney (A) as evidenced by Szebenyi (U).

Wozney discloses a composition comprising BMP-6 and k-fibroblast growth factor (kFGF) (column 8, full paragraph 1), wherein the composition additionally comprises collagen (paragraph bridging columns 8-9). k-FGF is an alternate name for FGF-4, as evidenced by Szebenyi (Table I).

10

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

15 obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wozney (A) as evidenced by Szebenyi (U).

Wozney discloses a composition comprising BMP-6 and k-fibroblast growth factor (kFGF) (column 8, full paragraph 1), wherein the composition additionally comprises collagen (paragraph bridging columns 8-9). k-FGF is an alternate name for FGF-4, as evidenced by Szebenyi (Table I).

25

Wozney as evidenced by Szebenyi is silent with respect to the molar ratio of BMP-6 to k-FGF. However, differences in concentration or temperature will not support

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the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. The invention is prima facie obvious over

5 the prior art.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

10 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply

15 with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to or encompass a composition comprising BMP-6 and FGF-4. The only disclosed use for the claimed composition is for the induction of

20 cardiogenesis in non-precordial cells, preferably human cells. The work done in the present specification was done with embryonic tissue. In the examples described the compositions that were shown to induce cardiogenesis in non-precordial cells included FGF-4 with BMP-2, and FGF-2 with BMP-2, BMP-4, BMP-7, BMP-6 or BMP-12. It is anticipated that FGF-4 can also work with BMP-4, BMP-7, BMP-6 or BMP-12 to induce

25 cardiogenesis. Paragraph bridging pages 3-4. There are no working examples in the present specification of the induction of cardiogenesis in non-precordial cells with the

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combination of BMP-6 and FGF-4. Furthermore, there is a lack of predictability in the art. Vukicevic (24, cited by Applicants) discloses that isoform specific differences exist in the role of the BMPs in embryonic tissue induction. OP-1 (BMP-7) induced markers of nephrogenic differentiation whereas closely related BMP-2 and TGF- $\beta$ 1 had no effect (page 9023, paragraph bridging columns 1-2). Vukicevic establishes that very similar proteins in the TGF- $\beta$  superfamily have opposite and/or unpredictable effects. Szebenyi discloses that the effects of FGFs on cellular functions depend on the biochemical state and environment of their target cell (page 46, full paragraph 1). Szebenyi establishes that what holds true for one FGF under one set of conditions does not hold true for the same FGF under another set of conditions. In view of the lack of working examples, the unpredictable effects of BMPs, and the conditions dependent effects of FGFs, the present specification has not enabled the claimed composition comprising BMP-6 and FGF-4 for the only disclosed use, i.e., the induction of cardiogenesis in non-precordial cells. It would require undue experimentation for the skilled artisan to practice the full scope of the claimed invention.

### ***Specification***

The disclosure is objected to because of the following informalities: In the continuing data on page 1 of the specification there is no year after "August 13."

Appropriate correction is required.

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***Conclusion***

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (571) 272-0887.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHT FAX NUMBERS:

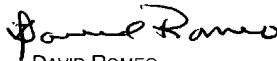
BEFORE FINAL (703) 872-9306

AFTER FINAL (703) 872-9307

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

DSR  
APRIL 30, 2004